Global Alliance
for Genomics & Health
Collaborate. Innovate. Accelerate.

BRCA Challenge
GA4GH Demonstration project in collaboration with ENIGMA
Initiated 2014 by Sir John Burn, Newcastle University & Stephen Chanock, National Cancer Institute
Current “Driver” team:
Amanda Spurdle – QIMR Berghofer Medical Research Institute, Brisbane
Gunnar Raetsch - ETH Zurich
David Goldgar, Sean Tavtigian - Huntsman Cancer Institute, University of Utah, Salt Lake City
Melissa Cline, Benedict Paten - University of California, Santa Cruz
Rachel Liao – Broad Institute, Cambridge, Massachusetts
BRCA Challenge – Institutions: Steering Committee

International representation

John Burn, Newcastle University, Newcastle upon Tyne, UK
Stephen Chanock, National Cancer Institute, Rockville, USA
Antonis Antoniou, University of Cambridge, Cambridge, UK
Larry Brody, National Human Genome Research Institute, Bethesda, USA
Robert Cook-Deegan, Duke University, Durham, USA
Fergus Couch, Mayo Clinic, Rochester, USA
Johan den Dunnen, Leiden University Medical Center, Leiden, Netherlands
Susan Domchek, University of Pennsylvania, Philadelphia, USA
Douglas Easton, University of Cambridge, Cambridge, UK
William Foulkes, McGill University, Montreal, Canada
Judy Garber, Dana-Farber Cancer Institute, Boston, USA
David Goldgar, Huntsman Cancer Institute, Salt Lake City, USA
Kazuto Kato, Osaka University, Osaka, Japan
Delyth Jane Morgan, Breast Cancer Now, Cancer Research UK

Robert Nussbaum, University of California San Francisco, USA
Kenneth Offit, Memorial Sloan Kettering Cancer Center, New York, USA
Sharon Plon, Baylor College of Medicine, Houston, USA
Gunnar Rätsch, ETH Zurich, Zurich, Switzerland
Nazneen Rahman, Institute of Cancer Research, London, UK
Heidi Rehm, Harvard Medical School, Boston, USA
Mark Robson, Memorial Sloan Kettering Cancer Center, NY City, USA
Wendy Rubinstein, National Institute of Health, Bethesda, USA
Amanda Spurdle, QIMR Berghofer Medical Research Institute, BNE, Australia
Dominique Stoppa-Lyonnet, Curie Institute, Paris, France
Sean Tavtigian, Huntsman Cancer Institute, Salt Lake City, USA
David Haussler, UC Santa Cruz Genomics Institute, Santa Cruz, USA
Bartha Knoppers, McGill University, Montreal, Canada
BRCA Challenge – Institutions across the globe
BRCA Challenge – Project Overview

● **Mission:** Improve care of patients at risk of breast and ovarian cancer using global data sharing and collaboration in the analysis of *BRCA1* and *BRCA2*
  1. Share *BRCA1* and *BRCA2* variants publically via a web portal
  2. Address social, ethical, legal challenges to global data sharing
  3. Create a GA4GH model for all disease genes

● **Clinical Focus:** Germline variant classification

● **Major milestones:**
  – BRCA Exchange - >17,900 variants, multiple sites
  – 1/3 expert-classified with supporting rationale
  – coming soon... mobile app with alert function
Features:

- Flexible searching
- Drill down to extra info
  - Tiled format
- Versioning...
  - Variant level
  - Dataset level
BRCA Challenge Mobile App

Gunnar Raetsch & Faisal Alquaddoomi

Features:

● Simplified presentation

● Follow a variant functionality (in testing phase)
BRCA Challenge – Goals & Previous Engagement

● **Goals:**
  * Variant level data – classification, rationale, other
  * Individual level data – clinical info, differing access
  * Algorithms to automate collection/classification

● **Previous Engagement with GA4GH:**
  * Ethics & regulatory:
    - FDA guidance (NGS testing & public variant databases)
    - Ethics WG chairs - database liability pub (GIM 19: 839)
  * Data WG: Adopted the GA4GH API
    - To allow others to access BRCA-Exchange data
  * ..... currently integrating with the Beacon network
• Genomic Knowledge & Clinical/Phenotype data
  • genomic nomenclature “translation”
  • associated clinical information/phenotype
    - including patient ascertainment
  • genetic & clinical data provenance/quality
• Data use & Researcher IDs - view & re-use of data
  • for clinical/research purpose
  • open access vs controlled (how much/who)
• Cloud - interoperability
  • optimising workflow, GA4GH approval stamp
• Discovery - controlling for overlapping data
BRCA Challenge – What we can offer to GA4GH?

- Feedback of BRCA Challenge developments
  - Algorithms for automated variant prioritization/classification
  - Field testing of standards on variant representation and clinical data
  - Mobile app for variant view and classification updates
Q&A

Gunnar, Benedict & Melissa to chime in!